1. (Currently amended) A method of screening for an agent to determine its usefulness in treating insulin resistance, the method comprising:

a) ~~establishing a paradigm in which at least one protein is differentially expressed in relevant tissue from, or representative of, subjects having differential levels of insulin sensitivity~~; identifying proteins which are differentially expressed in biological samples obtained from insulin resistant, normal or insulin sensitive subjects in response to a known treatment or compound which alters insulin sensitivity

b) providing ~~obtaining~~ a biological sample comprising cellular tissue or a subcellular fraction thereof susceptible to insulin action ~~of relevant tissue taken from, or representative of an insulin resistant subject, who or which has been treated with an agent being screened~~;

c) contacting the sample of step b) with said agent and identifying proteins which are differentially expressed in response to said agent; and

d) comparing the results of a) and c) thereby identifying those agents which alter the expression levels of said proteins towards that observed in an insulin resistant or insulin sensitive subject. ~~determining the presence, absence or degree of expression of the differnentially expressed protein or proteins in the tissue from, or respresentative of, the treated subject; and~~

~~d) selecting or rejecting the agent according to the extent to which it changes the expression, activity or amount of the differentially expressed protein or protein in the treated insulin resistant subject~~.

2. (Original) The method of claim 1, wherein the agent is selected it if changes the expression of the differentially expressed protein or proteins towards that of a normal subject or a more insulin sensitive subject.

3. (Original) The method of claim 2, wherein the agent is selected if it converts the expression of the protein or proteins to that of a normal or more insulin sensitive subject.

4. (Currently amended) The method of claim 1, wherein ~~in the paradigm,~~ the subjects of step a) ~~having differential levels of insulin sensitivity~~ comprise normal subjects and insulin resistant subjects.

5. (Currently amended) The method of claim 1, wherein ~~in the paradigm~~ the subjects of step a) ~~having differential levels of insulin sensitivity~~ comprise normal subjects and abnormally insulin sensitive subjects.

6. (Original) The method of claim 5, wherein the abnormally insulin sensitive subjects have acquired higher than normal sensitivity by exercise.

7. (Previously presented ) The method of claim 1, wherein the relevant tissue is liver, skeletal muscle, white or brown adipose tissue.

8-13. (Cancelled)

14. (Currently amended) The method of claim 1, wherein ~~in the paradigm~~ the insulin-resistant subjects of step a) are animals which are insulin-resistant as a result of genetic mutation, and the normal subjects are normal control animals.

15. (Original) The method of claim 14, wherein the normal control animals are insulin sensitive littermates of the genetically mutated animals.

16. (Currently amended) The method of claim 1, wherein ~~the paradigm is established in tissue from, or representative of,~~ the test subjects of step a) are animals which are insulin-resistant as a result of diet, and the normal subjects are normal control animals.

17. (Currently amended) The method of claim 1, wherein ~~in the paradigm~~ the normal and insulin resistant subjects of step a) are animals which are insulin-sensitive on a natural diet, but develop insulin resistance when given an unnatural, laboratory diet.

18. (Currenty amended) The method of claim 1, wherein ~~in the paradigm~~ the treatment to increase the level of insulin sensitivity comprises treatment with an insulin-sensitising drug.

19. (Original) The method of claim 18, wherein the insulin sensitizing drug is thiazolidinedione.

20. (Original) The method of claim 19, wherein the thiazolidinedione is rosiglitazone (BRL 49653).

21. (Original) The method of claim 18, wherein the insulin sensitizing drug is a non-thiazolidinedione which is (a) an agonist or partial agonist of the PPAR gamma nuclear receptor, (b) a b3-adrenoceptor agonist or (c) a leptin or leptin fragment.

22. (Currently amended) The method of claim 1, wherein ~~in the paradigm~~ the treatment to increase the level of insulin sensitivity comprises dietary restriction and/or exercise.

23. (Currently amended) The method of claim 1, wherein the sample ~~obtained~~ of step b) is taken from ~~or is representative of~~ a subject suffering from non-insulin dependent diabetes.

24. (Currently amended) The method of claim 1, wherein the sample of step b) is taken from ~~or is representative of~~ a subject suffering from polycystic ovary syndrome, syndrome X, insulin resistance syndrome or type I diabetes.

25. (Currently mended) The method of claim 1, wherein ~~the paradigm is established~~ the differentially expressed proteins are identified by two-dimensional gel electrophoresis carried out on the relevant tissue or a protein-containing extract thereof.

26. (Cancelled)

27. (Previously presented) The method of claim 1, further comprising the step of isolating at least one of the differentially expressed protein identified in the method.

28. (Original) The method of claim 27, further comprising the step of characterizing the isolated protein.

29. (Previously presented) The method of claim 1, wherein the differentially expressed protein or proteins comprises one or more of LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30, MOM31, MOM32, MOM33, MOMT34, MOMT35, MOM36, WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64, WSEM65, BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77.

30. (Original) The method of claim 28, further comprising using the protein in an assay for specific binding partners of the protein.

31. (Original) The method of claim 28, further comprising using the protein in an assay to screen for agonists or antagonists of the protein.

32. (Previously presented) The method of claim 1, wherein the agents or proteins are screened using a high throughput screening method.

33. (Previously presented) A method of making a pharmaceutical composition which comprises having identified an agent using the method of claim 1, the further step of manufacturing the agent and formulating it with an acceptable carrier to provide the pharmaceutical composition.

34. (Original) A protein for use in a method of medical treatment, wherein the protein is selected from LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30, MOM31, MOM32, MOM33, MOMT34, MOMT35, MOM36, WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64, WSEM65, BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77

Claims 35-37 (Cancelled)

38. (Previously presented) A method of treating a condition characterised by insulin resistance in a patient, the method comprising administering a therapeutically or prophylactically effective amount of such an agent identified by a method of claim 1 to the patient.

39. (Original) A method of determining the nature or degree of insulin resistance in a sample of relevant tissue from a human or animal subject, which comprises:

a) establishing a paradigm in which at least one protein is differentially expressed

in relevant tissue from, or representative of, subjects having differential levels of insulin sensitivity;

b) obtaining a sample of the tissue and

c) determining the presence, absence or degree of expression of the differentially expressed protein or proteins in the sample, and

d) relating the determination to the nature or degree of the insulin resistance by reference to a previous correlation between such a determination and clinical information.

40. (Original) The method of claim 39, wherein in the paradigm at least four protein are differentially expressed, providing a multi-protein finger print of the nature or degree of insulin resistance.

41. (Previously presented) The method of claim 39, wherein in the paradigm the subjects having differential levels of insulin sensitivity comprise normal subjects and insulin resistant subjects.

42. (Previously presented) The method of claim 39, wherein the subjects having differential levels of insulin sensitivity comprise normal subjects and subjects having abnormally high insulin sensitivity.

43. (Previously presented) The method of claim 39, which further comprises determining an effective therapy for treating the abnormality.

44. (Previously presented) The method of claim 39, wherein the sample is taken from a patient undergoing treatment for the insulin resistance and wherein the method further comprises monitoring the treatment.

45. (Original) A protein which is differentially expressed in relevant tissue from or representative of subjects having differential levels of insulin sensitivity and which is obtainable by the method of two-dimensional gel electrophoresis carried out on said tissue or a protein-containing extract thereof, the method comprising:

a) providing non-linear immobilized pH gradient (IPG) strips of acrylamide polymer 3 mm x 180 mm;

b) rehydrating the IPG strps in a cassette containing 25 ml. of an aqueous solution of urea (8M), 3- [(cholamidopropyl) dimethylammonio]-1-propanesulphonate (CHAPS, 2% w/v), dithioerythritol (DTE, lOmM), mixture of acids and bases of pH 3.5 to 10 (2% w/v) and a trace of Bromophenol Blue;

(c) emptying the cassette of liquid, transferring the strips to an electrophoretic tray fitted with humid electrode wicks, electrodes and sample cups, covering the strips and cups with low viscosity paraffin oil;

(d) applying 200 micrograms of an aqueous solution of dried, powdered material of the relevant body tissue in urea (8M), CHAPS (4% w/v), Tris (40 mM), DTE (65 mM), SDS (0.05% w/v) and a trace of Bromophenol Blue to the sample cups, at the cathodic end of the IPG strips;

(e) carrying out isoelectric focusing on the gel at a voltage which increases linearly from 300 to 3500 V during 3 hours, followed by another 3 hours at 3500 V, and

thereafter at 5000V for a time effective to enable the proteins to migrate in the strips to their pI- dependent final positions;

(f) equilibrating the strips within the tray with 100 ml of an aqueous solution containing Tris-HCl (50 mM) pH 6.8, urea (6M), glycerol (30% v/v), SDS (2% w/v) and DTE (2% w/v) for 12 minutes;

(g) replacing this solution by 100 ml. of an aqueous solution containing Tris-HCl (50 mM) pH 6.8, urea (6M), glycerol (30% v/v), SDS (2% w/v), iodoacetamide (2.5% w/v) and a trace of Bromophenol Blue for 5 minutes ;

(h) providing a vertical gradient slab gel 160 x 200 x 1.5 mm of acrylamide/piperazine-diacrylyl cross- linker (9-16% T/2. 6% C), polymerised in the presence of TEMED (0.5% w/v), ammonium persulphate (0.1% w/v) and sodium thiosulphate (5 mM), in Tris-HCl (0.375M) pH 8.8 as leading buffer ;

(i) over-layering the gel with sec-butanol for about 2 hours, removing the overlay and replacing it with water;

(j) cutting the IPG gel strips to a size suitable for the second dimensional electrophoresis, removing 6 mm from the anode end and 14 mm from the cathode end;

(k) over-layering the slab gel with an aqueous solution of agarose (0.5% w/v) and Tris-glycine-SDS (25 mM-198 mM-0.1% w/v) as leading buffer, heated to 70°C and loading the IPG gel strips onto the slab gel through this over-layered solution;

(l) running the second dimensional electrophoresis at a constant current of 40 mA at 8-12°C for 5 hours; and

(m) washing the gel.

46. (Original) A differentially expressed protein of claim 45 as obtainable from mouse liver cells of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein LOM16, LOM17, LOM18, LOMT19, LOM20, LOMT21, LOMT22, LOMT23, LOMT24, LOMT25, LOMT26, LOM27, LOM28, LOM29 or LSEM30.

47. (Original) A differentially expressed protein of claim 45 as obtainable from skeletal muscle cells of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein MOM31, MOM32, MOM33, MOMT34, MOMT35 or MOM36.

48. (Original) A differentially expressed protein of claim 45 as obtainable from white adipose tissue of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein WOMT37, WOM38, WOMT39, WOM40, WOM41, WOMT42, WOM43, WOM46, WOM47, WOMT48, WOMT49, WOMT50, WOM51 to 55, WOM57 to 64 or WSEM65.

49. (Original) A differentially expressed protein according to claim 45 as obtainable from brown adipose tissue of obese, insulin resistant mice, which may have been treated with rosiglitazone, and designated herein BOM66, BOM67, BOMT68, BOM69 to 75, BOMT76 or BOM77.

50. (Original) A differentially expressed protein having one or more of the identifying

characteristics set out in Table 1 to 4.

51. (Original) The differentially expressed protein of claim 50, wherein the identifying characteristics are pI and Mw.

52. (Previously amended) A method whereby the pattern of differentially expressed proteins in a tissue sample or body fluid sample of an individual with insulin resistance is used to predict the most appropriate and effective therapy to alleviate the insulin resistance and to monitor the success of that treatment.

53. (Previously presented) The method of claim 10, wherein the comparatively insulin sensitive subjects are normal subjects or abnormally insulin sensitive subjects.